REMARKS

The specification has been amended to correct inadvertent typographical and grammatical errors, and the claims have been amended to clarify the invention. In particular, the specification has been amended to correct inadvertent errors in referencing amino acid residues in SEQ ID NO:1 in the paragraph beginning at p. 10, line 30 of the specification. The correct residue designations are found in the Sequence Listing for SEQ ID NO:1. The paragraph beginning at p. 11, line 20 has also been amended to correct reference to the cDNA encoding Ankrd2V (SEQ ID NO:2) in the table as SEQ ID NO:3. Claim 1 has been amended to recite a specific antigenic epitope and a biologically active portion of SEQ ID NO:1, as well as a naturally occurring variant of SEQ ID NO:1 having at least 90% identity to SEQ ID NO:1. Support for the amendments to claim 1 is found in the specification, for example, at p. 10, line 33 through p. 11, line 3 (antigenic epitopes and biologically active portion of SEQ ID NO:1), and at p. 4, lines 22-23, and at p. 9, lines 22-28 (variants). Claim 11 has been amended to recite "A method of using a cDNA to screen a plurality of molecules or compounds for a molecule or compound that specifically binds the cDNA". No new matter is added by these amendments, and entry of the amendments is requested.

Status of the Application and Withdrawn Rejections

The Examiner has withdrawn the finality of the Office Action mailed on October 10, 2002 in order to rejoin and examine claims 7-12, as applicant requested. The Examiner stated further that the rejection of claims 1, 2, 4 and 5 under 35 U.S.C. § 102(a) and the rejection of claims 3 and 5 under 35 U.S.C. § 103(a) as set forth in the Office Action mailed May 1, 2002 has been withdrawn in view of applicants declaration under 37 CFR 1.131 submitted in the response filed November 19, 2002.

35 U.S.C § 112, First Paragraph, Rejection of Claim 10

The Examiner has rejected claim 10 under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of using the claimed cDNA for diagnosis of clear cell sarcoma, wherein the cDNA is highly expressed in a sample when compared with normal musculoskeletal tissues, does not reasonably provide enablement for a method of using a cDNA for the diagnosis of clear cell sarcoma wherein the cDNA expression is relatively lower. The Examiner stated that claim 10 is drawn to a method of using a cDNA to detect expression of a nucleic acid in a sample,

wherein the cDNA is differentially expressed when compared to a standard and diagnostic of clear cell sarcoma. However, the Examiner noted, the term "differentially expressed" encompasses both a higher degree of expression or a lower degree of expression when compared with the expression of the cDNA in normal musculoskeletal tissue, while it is apparent that only the higher degree of expression of the cDNA is diagnostic of clear cell sarcoma.

The Examiner also stated that it is unclear what a "standard" encompasses here in the instant claim. Without the unambiguously defined standard, one skilled in the art would not be able to perform the claimed method.

Applicants Response

With respect to the proper interpretation of the terms recited in a claim, Applicants submit that it is well known (and well established by case law) that the claims of an application are to be interpreted in light of the knowledge of one skilled in the art and the disclosures of the specification. "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." See MPEP § 2164.01. As the Examiner has noted, the term "differential expression" has been defined in the specification at p. 7, lines 20-21 as "---increased, upregulated---or decreased, downregulated---in a sample". Since the specification, as the Examiner has also noted, clearly describes the upregulation or increased expression of Ankrd2V in clear cell sarcoma of the skeletal muscle relative to normal muscle tissue, One skilled in the art would clearly interpret the use of the term "differentially expressed" as it is recited in the claim to refer only to the increased or upregulation of the gene in the diseased state.

With regard to the Examiner's alleged ambiguity of the use of the term "standard" in the claim, Applicants submit that the term has clear meaning in the art . Again, the term as recited in the claim, would be interpreted in light of the knowledge of one skilled in the art and the disclosures of the specification. Indeed, the Examiner has already noted that the specification discloses that the presence of clear cell sarcoma in muscle tissue is indicated where a higher degree of expression is observed when compared to normal musculoskeletal tissues, e.g., to a "standard". See Office Action, top of page 3. It is further noted that the specification states at p. 10, lines 23-29 that:

> "It is particularly noteworthy that although the transcript is highly expressed in a patient with clear cell sarcoma, it has low expression in liposarcoma and other cancers of muscle tissue. Therefore, the cDNA is useful in assays to distinguish between clear cell sarcoma and other cancers of muscle tissue"

The specification further describes the establishment of proper standards for comparison with samples for disease diagnosis in the two paragraphs beginning at p. 18, line 19 as follows.

> For example, the cDNA or probe may be labeled by standard methods and added to a biological sample from a patient under conditions for the formation of hybridization complexes. After an incubation period, the sample is washed and the amount of label (or signal) associated with hybridization complexes, is quantified and compared with a standard value. If complex formation in the patient sample is significantly altered (higher or lower) in comparison to either a normal or disease standard, then differential expression indicates the presence of a disorder.
>
> In order to provide standards for establishing differential expression, normal and disease expression profiles are established. This is accomplished by combining a sample taken from normal subjects, either animal or human, with a cDNA under conditions for hybridization to occur. Standard hybridization complexes may be quantified by comparing the values obtained using normal subjects with values from an experiment in which a known amount of a substantially purified sequence is used. Standard values obtained in this manner may be compared with values obtained from samples from patients who were diagnosed with a particular condition, disease, or disorder. Deviation from standard values toward those associated with a particular disorder is used to diagnose that disorder.

From these disclosures and the knowledge of one of skill in the art, a "standard" would clearly be understood to encompass any source of normal musculoskeletal tissue and that comparison with such a standard would indicate the presence of clear cell sarcoma only on observing a higher degree of expression of the gene. One of skill in the art would clearly know how to perform the claimed method from these disclosures without undue experimentation.

Applicants therefore submit that the claim as originally filed is fully enabled by the specification to one of skill in the art and request withdrawal of the rejection of claim 10 under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, Second Paragraph, Rejection of Claims 10-12

The Examiner has rejected claims 10-12 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner stated that claim 10 is indefinite because the metes and bounds of the term "standard" is unclear. As applicants have discussed above under the rejection of this claim under 35 U.S.C § 112, first paragraph, one of skill in the art would clearly understand the meaning of the term as it is recited in the claim in light of the specification and the knowledge of one skilled in the art, and would therefore understand its metes and bounds as used in the claim.

The Examiner stated that claim 11 is indefinite because the preamble of the claims is ambiguous. It appears that the method is intended to be drawn to a method of using a cDNA to screen a plurality of molecules for those that bind the cDNA, and that an amendment accordingly would overcome this rejection. Claim 11 has been amended to recite "A method of using a cDNA to screen a plurality of molecules or compounds for a molecule or compound that specifically binds the cDNA".

The Examiner stated that claim 11 is indefinite because the steps set forth in the methods do not necessarily achieve the goal of identifying cDNA-binding compounds. It is unclear, the Examiner stated, how a single compound that binds a cDNA can be identified by the two claimed steps, combining the cDNA with a plurality of molecules and detecting their binding.

The term "specific binding" is well understood in the art as are specific methods of measuring such binding. In addition, however, the specification defines the term as it is used in the application at p. 9, lines 6-9, and gives examples of such binding as they apply to the claimed method. An example of screening techniques for measuring specific binding is further disclosed in the specification at p. 36, lines 21-29. Given these disclosures, together with that which is well known in the art regarding the measurement of "specific binding", the two steps reciting ; a) combining the cDNA of claim 1 with a plurality of molecules or compounds under conditions to allow specific binding (underline added); and b) detecting specific binding, thereby identifying a molecule or compound which specifically binds the cDNA, is sufficient for one of skill in the art to achieve the stated objective of the claim .

The Examiner stated that claim 12 is indefinite because it recites "peptide nucleic acids", "repressors", and "regulatory molecules" and it is unclear what the metes and bounds of these terms are. Applicants submit that these terms are well known to one of skill in the art and are used accordingly throughout the specification. The specification further describes these and related categories of molecules that would be of likely interest for testing as specific binding agents in methods of screening recited in claims 11 and 12 at p.20, lines 27-30 as follows:

> "The cDNA encoding Ankrd2V may be used to screen a library of molecules or compounds for specific binding affinity. The libraries may be aptamers, DNA molecules, RNA molecules, PNAs, peptides, proteins such as transcription factors, enhancers, repressors, and other ligands which regulate the activity, replication, transcription, or translation of the cDNA in the biological system.".

From these descriptions and the knowledge of one skilled in the art, suitable libraries of these agents would be readily apparent to one of skill in the art for use in such a screening assay.

With the above amendments and arguments, applicants believe that claims 10-12 are clear and definite, and therefore request withdrawal of the rejection of these claims under 35 U.S.C. 112, second paragraph.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Agent of Record, below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION.

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